Amendments to the Drawings

The attached sheets of drawings include changes to FIG. 5, FIG. 9, and FIG. 10. These sheets which include FIG. 5, FIG. 9, and FIG. 10, replace the original sheets including FIG. 5, FIG. 9, and FIG. 10. The Examiner is advised that FIG. 9, FIG. 10, FIG. 11, and FIG. 12 were filed in a Response to Missing Parts on November 12, 2004.

In FIG. 5, the x-axis label "Time in Minutes (min)" and the y-axis label "CPM" have been added.

In FIG. 9, the x-axis label "Time in Minutes (min)" has been added.

In FIG. 10, the x-axis label "Time in Minutes (min)" has been added.

REMARKS

The Applicants respectfully rebut the Examiner's statement, "Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a))." The Applicants direct the Examiner's attention to the Response to Restriction Requirement mailed January 14, 2005, page 4. The Applicants state, "All pending claims are currently directed to novel methods of inhibiting bacterial infection using bactericidal SPO1 proteins. The generic claim to methods of inhibiting bacterial infections includes a Markush group of SPO1 peptides which are active antibacterial peptides SEQ ID NO: 1-5, 7-10, and 12-24. The Applicants have **provisionally elected** a single species, SEQ ID NO: 8 (GENE 44)." (*emphasis added*). Furthermore the Applicants reference MPEP §803.02, see Footnote 1, which covers Markush-type claims and **provisional election** of species.

Practice Re Markush-Type Claims

MPEP §803.02 states, "If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made **without serious burden**, the Examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the Examiner will not follow the procedure described below and will not require restriction." Applicants point out that the Examiner can search **all** of the sequences (SEQ ID NO.: 1-24) at **one time** using GenBank Accession # AF031901 as disclosed in the specification. This would not place an undue burden on the Examiner.

Further, MPEP §803.02 states, "unity of invention exists where compounds included within a Markush group (1) share a **common utility**, and (2) share **a substantial structural feature** disclosed as being essential to that utility." The claimed methods of inhibiting bacterial infection with peptides sharing a common **"antimicrobial" utility** and a common **"SPO1" structural feature**.

Finally, MPEP §803.02 states, "the Examiner may require a **provisional** election of a single species prior to examination on the merits. The provisional election will be given effect in the event that the Markush-type claim should be found not allowable. Following election, the Markush-type claim will be examined fully with respect to the elected species and further to the extent necessary to determine patentability. If the Markush-type claim is not allowable over the prior art, examination will be limited to the Markush-type claim and claims to the elected species, with claims drawn to species patentably distinct from the elected species held withdrawn from further consideration."

The Applicants respectfully request that the Examiner treat the Markush group as **provisionally elected** species SEQ ID NO: 8. According to MPEP §803.02, upon allowance of the elected species, the Examiner should expand the scope of the search to determine patentability of additional members of the Markush Group. Should the Examiner determine additional members of the Markush Group are allowable, the claims should be allowed to stand. If the Examiner finds arguments against the allowability of one or more members of the Markush Group the claims shall be amended accordingly.

The Applicants respectfully request the Examiner contact them if there are any questions or procedures that need to be addressed.

ARGUMENTS

ENABLEMENT

Claims 11-12, 19 and 21 were rejected under 35 U.S.C. §112 as not enabled and not described. The Applicants have provided all of the methods required to generate peptidomimetic small molecules using the antimicrobial SPO1 peptides. While not conceding the Examiner's argument, the Applicants have amended the claims making the rejection moot.

OBVIOUSNESS

Claims 11-15 and 17-21 were rejected under 35 U.S.C. §103(a) as obvious in light of Wei, et al. (1993). The Examiner has not established a *prima facia* case of obviousness as set forth by MPEP §2143.

Prior Art Does Not Teach "inhibiting bacterial infection ... in a mammal"

To establish *prima facia* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. (MPEP § 2143.03). The prior art does **not** describe "inhibiting bacterial infection ... in a mammal" by "identifying the presence of a bacteria in a mammal" and "administering to said mammal a protein ..." Because the prior art reference does not provide these elements of the claimed invention, the Examiner has failed to prove a *prima facia* case of obviousness.

No Motivation to Modify to "inhibit a bacterial infection ... in a mammal"

The level of skill in the art cannot be relied upon to provide the suggestion to combine references (MPEP § 2143.01). There is no motivation in Wei to modify the reference to "inhibit a bacterial infection ... in a mammal." The Examiner has provided no additional motivation to modify Wei to "inhibit a bacterial infection ... in a mammal" other than the Examiner's statement. Because there is no motivation in Wei to use the *e3*/gene 44 protein for treatment of bacterial infections **in a mammal** and no additional motivation is provided to treat bacerial infections in a mammal, the Examiner has failed to prove a *prima facia* case of obviousness.

Unexpected Synergies of Combinations of SPO1 Peptides

Presence of a property not possessed by the prior art is evidence of nonobviousness. (MPEP § 716.02 (a)). The Examiner **admitted** that "**unexpected results** of the protein combinations provide increased bactericidal activity that would be unobvious to a skilled artisan." The combination of gene 44 (SEQ ID NO: 8) with gene 50 (SEQ ID NO: 14) and/or gene 51 (SEQ ID NO: 15) were specifically identified by the Examiner as unexpected. Other combinations in Table 2 on page 12, including GP50/51, GP38/39/40, GP45/46, GP53/54/55, GP52/53/54/55, GP56/57/59, and GP59/60, showed

synergistic effects as described in the specification. The Applicants request that claims 13, 14 and 22-28 be allowed as the synergistic benefits of combining SPO1 proteins is unexpected and unobvious.

Long-felt but unsolved need to control the Herxheimer reaction

Evidence of criticality including long-felt but unsolved needs and failure of others must be considered by the Examiner in determining the issue of obviousness of claims for patentability under 35 U.S.C. 103. The antimicrobial genes and peptides described herein solve problems associated with the Herxheimer reaction, the liberation of endotoxins as a consequence of widespread lysis of bacteria in the body, because each of them kills without lysing the bacterial cell as stated in the specification, page 3 ¶10. This has been documented directly for several of the genes by showing either microscopically or turbidimetrically that the structure of the cells remains intact even after they have lost viability. Specification page 23 ¶92. Because lysis of bacteria in a mammal cause the Herxheimer reaction, the use of Gene 44 and combinations of Gene 44 and other SPO1 peptides to "inhibit a bacterial infection ... in a mammal" solves problems previously associated in mammals with the Herxheimer reaction during antibacterial treatments.

Prior Art Teaches Away from GP44 being the Optimum Antimicrobial Protein

A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. (MPEP § 2141.02). Wei, et al. (1993) actually teach away from using the *e3*/gene 44 product as "DNA, RNA, and protein synthesis were shut off to approximately the same extent by the mutant [*e3* truncation] as by wild-type SPO1." Further, the Wei reference cites the possibility of "at least 12, and possibly as many as 20, active early genes of unknown function." Finally, Wei states, "The fact that shutoff can be caused by *e3* expression in uninfected cells is not sufficient to show that E3 is responsible for the shutoff that occurs during SPO1 infection." Because there is uncertainty in the Wei reference about the function and redundancy in the SPO1 early genes and which SPO1 protein would provide a treatment

of bacterial infection in a mammal, the Wei reference teaches away from a method "inhibit a bacterial infection ... in a mammal."

CONCLUSION

Simply identifying a cytotoxic early gene from SPO1 does not outweigh the uphill battle required to "inhibit a bacterial infection ... in a mammal." The cited art does not provide the elements of "inhibiting a bacterial infection ... in a mammal," does not provide a motivation to "inhibit a bacterial infection ... in a mammal," and teaches away from the identity of proteins for use in treatment of bacterial infections in a mammal. The unexpected synergies of combinations of SPO1 proteins are unobvious to one of skill in the art and the treatement of antibacterial infections in a mammal with SPO1 peptides and combinations thereof address the long-felt but unsolved need to control the Herxheimer reaction.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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Respectfully submitted,

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